REMARKS

Claims 13, 18, 23, and 25 have been canceled. Claims 1, 3, 6-8, 14-17, and 19-22 have been amended. New claims 26 and 27 have been added. No new matter has been added. Upon entry of this amendment, Claims 1, 3, 6-8, 14-17, 19-22, 24, and 26-27 will be pending in the application. Reconsideration of the claims in light of the above amendment and the following remarks is respectfully requested.

Antibodies 595A6 and BM7

The Examiner indicated that a typographical error appeared to have occurred such that "BM7" was replaced with "595A6". The Examiner also required that claims 3 and 16 be amended to replace "595A6" with "BM7" to avoid problems with new matter and to be consistent with an election as a result of the prior restriction requirement. Such amendments have been made.

Claim Rejections - 35 U.S.C. § 112, 1st ¶

Claims 1, 3 and 6-8

Claims 1, 3 and 6-8 remain rejected under 35 U.S.C. 112, first paragraph for reasons set forth in Paper No. 13, Section 6, pages 3-6 and in Paper No. 17, Section 4, pages 2-3. Applicants respectfully traverse the rejection.

The Office Action (Paper No. 20) states, "Applicant has speculated, without *in vivo* experimentation, that due to high specific activity of the disclosed immunotoxins *in vitro* it seems possible to administer the mixture for *in vivo* treatment of patients suffering from different types of carcinoma."

The Examiner further stated, "in the absence of a demonstration of the efficacy of the method in an appropriate animal model" one skilled in the art would not believe that the claimed method would be effective *in vivo*. The Examiner appears to have mistakenly concluded that the application is devoid of data from *in vivo* experimentation supporting the claimed method. Examples 3 and 4 at pages 26-28 of the application, for example, show efficacy of immunotoxins, MOC31-PE and BM7-PE, in an appropriate animal model. In these examples, intravenously administered immunotoxins increased survival time of rats injected with human

breast cancer cells lines into the left cardiac ventricle and into bone marrow. As additional support for the proposition that the immunotoxins MOC31-PE and BM7-PE are effective in an appropriate *in vivo* model, Applicant submits herewith a copy of a journal article (Int. J. Cancer 88: 970-976, 2000) demonstrating the effectiveness of the immunotoxins in a nude rat model. One skilled in the art would understand the effectiveness of the claimed invention given the *in vivo* data in the application showing the effectiveness of the individual immunotoxins in rat models in combination with the *in vitro* data showing 1) the high specificity of the antibodies, 2) the effectiveness of the combined immunotoxin approach, and 3) the low toxicity of the combined immunotoxin approach for non-maligant cells. This combination of *in vitro* and *in vivo* data reaches well beyond speculation. One skilled in the art would understand that two immunotoxins, each independently effective in vivo, would be effective in combination, especially if *in vitro* studies showed the combination to be surprisingly effective.

The Examiner also stated, "even if *in vitro* data were convincing, this single example [apparently referring to the combination of MOC31-PE and BM7-PE] would not be sufficient to enable the broadly claimed invention."

Claim 1, from which claims 3 and 6-8 depend, has been amended to so that they are directed to methods "to kill breast cancer cells or other carcinoma cells expressing the same target antigens" rather than "to kill breast cancer cells or other carcinoma cells expressing target antigens." This amendment which clarifies the previous claim clearly shows that the claims are enabled by the specification. As indicated above, the application demonstrates not only *in vitro* effectiveness but also *in vivo* effectiveness of immunotoxins useful for the claimed method against breast cancer cells. One skilled in the art would expect that other cells expressing the same antigens, EGP2 and MUC1, would be similarly affected. The combination of *in vitro* and *in vivo* data in the application revealing the effectiveness of immunotoxins directed to EGP2 and MUC1 antigens would enable one skilled in the art to make and use the invention commensurate in scope with the claims.

Applicant asserts that the claimed invention is enabled by the specification. In light of the above remarks, Applicant respectfully requests withdrawal of this rejection.

Claim 3

Claim 3 remains rejected for the reasons previously set forth in Paper No. 13, Section 7, pages 6-9 and in Paper No. 16, Section 5, page 4. The Office Action (Paper No. 20) indicates that a website from which BM7 could be obtained is not objective evidence that BM7 is commercially available. Applicant respectfully traverses the rejection.

Applicant fails to understand why a website offering information of a product and contact information for purchase of the product is not sufficient objective evidence of commercial availability of the product. Applicant again asserts that the monoclonal antibody BM7 can be obtained from:

MEDAC GmbH
Postfach 303629
D-20312 HAMBURG GERMANY
tel: 040/350920-0
fax: 040/350902-61

In the response to the previous office action, Applicant included an URL to the MEDAC website that was in German. The English language version of the website can be found at <http://www.medac.de/medac-e/index.html>. Information regarding BM7 can be obtained at this website under "product portfolio" -> "diagnostics" -> "products" -> "oncology".

Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections - 35 U.S.C. § 112, 2nd ¶

Claims 1, 3, 6-8 and 14 remain rejected under 35 USC 112, second paragraph for the reasons previously set forth in paper No 13, Sections 8c and 8g, pages 10-11 and in Paper No. 16, Section 6, pages 4-5. Applicant traverses the rejection to the extent that it is maintained.

In Paper No. 16, the claims were rejected because claim 1 recited, "fragments thereof." Claim 1 has been amended to recite "antibody binding fragments" and "active toxin fragments" as suggested by the Examiner in Paper No. 13, at Section 8c, page 10.

In Paper No. 16, the claims were rejected to for reciting the designations "BM7" and "MOC31" because no evidence of public availability of these antibodies was presented. In Paper No. 13, at Section 8g, page 11, the claims were similarly rejected. Applicants assert that

evidence of public availability in this response and in Applicant's prior response has been presented with regard to both BM7 and MOC31.

In light of the amendment and above remarks, Applicants assert that the claims are definite. Withdrawal of the rejection is respectfully requested.

Claim Rejections - 35 U.S.C. § 103

Claims 1 and 14 remain rejected under 35 USC 103 for the reasons previously set forth in Paper No. 13, Section 10, pages 12-15 and Paper No. 16, Section 7, pages 5-7. That is, the claims stand rejected as allegedly being obvious over Lemoli et al. in view of Brugger et al., Parry et al., Bjorn et al., and US Patent No. 5, 185, 254. Applicants respectfully traverse the rejection.

The claimed method provides surprising efficacy against malignant cells, which would not be predicted by the references cited by the Examiner. None of the references cited by the Examiner alone or in combination suggest that the combination of immunotoxins directed to EGP2 and MUC1 would prove more effective than the sum of each immunotoxin directed to either EGP2 or MUC1 alone. The present application shows this unexpected result (see, for example, page 11, lines 14-17 and table 4). The unexpected advantages of the claimed method were neither taught nor suggested by the references cited by the Examiner, alone or in combination. Because of the unexpected and surprising advantages of the claimed method over the art cited by the Examiner, Applicant asserts that the claimed invention is not obvious. Withdrawal of the rejection is respectfully requested.

New Grounds of Objection - Specification

The Office Action (Paper No. 20) indicates that the specification was objected to as failing to provide proper antecedent basis for the claimed subject matter. Specifically, the Examiner stated that claims 1, 3, 6-8, and 14 are drawn to toxin fragments while the specification is lacking support for the claimed toxin fragments. Applicant traverses the rejection to the extent that it is maintained.

The specification has been amended to recite "toxin fragments." No new matter has been added as the originally filed claims provided support for such an amendment. For example, claim 1 as originally filed recited, "fragments of antibodies and toxin, or recombinantly produced

antibodies, toxins, immunotoxins, or fragments thereof." In light of the amendment to the specification, withdrawal of the objection is respectfully requested.

New Grounds of Rejection - Claim Rejections - 35 U.S.C. § 112

Claims 3 and 16

Claims 3 and 16 have been rejected under 35 USC 112, first paragraph, because 1) the claims recite "595A6" antibody without support in the specification and 2) the specification does not provide evidence that "595A6" antibody is publicly available, reproducible form the written description, or deposited. Applicant traverses the rejection to the extent that it is maintained.

Claims 3 and 16 have been amended to replace "595A6" with "BM7," which, as stated above, is commercially available and supported by the specification. Withdrawal of the rejection is respectfully requested.

Claims 15-21 and 25

Claims 15-21 and 25 have been rejected under 35 USC 112, first paragraph, as lacking a written description of the claimed invention. Applicant traverses the rejection.

The Examiner stated that the limitations "at least two immunotoxins" and "two or more immunotoxins" as recited in claims 15 and 21, respectively, have no clear support in the specification. Applicant asserts that the one of skill in the art would understand, upon reading the specification, would understand that two or more immunotoxins could be successfully used with a method according to the claimed invention. This is because the specification at page 4 lines 8-10 states:

> The present invention relates to purging of harvested stem cell populations in cases of solid tumors in which the cell population is exposed to a composition of two or more antibodies connected to bacterial toxins.

Accordingly, claims 1, 15, 21, and 22 now specifically recite "two or more immunotoxins" to be consistent with the language of the specification. Withdrawal of the rejection is respectfully requested.

Claims 15-20 and 22-24

Claims 15-20 and 22-24 have been rejected under 35 USC 112, first paragraph, as lacking a written description of the claimed invention. Applicant traverses the rejection.

The Examiner stated that the limitation "a method for killing malignant cells" recited in claims 15 and 22 has no support. Claims 15 and 21 have been amended to recite, "a method for killing breast cancer cells or other carcinoma cells expressing the same antigens." The specification has been amended to recite this language, which was in originally filed claim 1. Additionally, the specification at, for example at page 11, lines 1-29, indicates that antigens expressed by GA733-2 and MUC1 can be found on cells from a variety of different tissues and carcinomas. Applicant asserts that the specification supports the claims as amended. Withdrawal of the rejection is respectfully requested.

Claims 1, 3, 6-8, 14, 21 and 25

Claims 1, 3, 6-8, 14, 21 and 25 have been rejected under 35 USC 112, first paragraph, as lacking a written description of the claimed invention. Applicant traverses the rejection to the extent that it is maintained. Applicant traverses the rejection.

The Examiner stated that the limitation "other carcinoma cells expressing target antigens" has no support. The calims have been amended to recite, "other carcinoma cells expressing the same antigens." The specification has been amended to recite this language, which was in originally filed claim 1. Additionally, the specification at, for example at page 11, lines 1-29, indicates that antigens expressed by GA733-2 and MUC1 can be found on cells from a variety of different tissues and carcinomas. Applicant asserts that the specification supports the claims as amended. Withdrawal of the rejection is respectfully requested.

Claims 15-17 and 19-20

Claims 15-17 and 19-20 have been rejected under 35 USC 112, first paragraph, as lacking a written description of the claimed invention. Applicant traverses the rejection to the extent it is maintained.

The Examiner stated that the limitation "a cell population" has no support but that there is support for "a cell population comprising peripheral blood cells (p.1, lines 5-10) or bone marrow cells (p. 1, line 26)." The claims have been amended to recite, "a cell population comprising

nucleated peripheral blood cells or bone marrow cells." Accordingly, withdrawal of the rejection is respectfully requested.

Claims 1, 3, 6-8 and 14-25

Claims 1, 3, 6-8 and 14-25 have been rejected under 35 USC 112, first paragraph, as lacking an enabling specification. Applicants traverse the rejection to the extent it is maintained.

The Examiner stated that the specification, "while being enabling for a method of killing breast cancer or other carcinoma cells which comprise the EGP2 and MUC1 antigens, does not reasonably provide enablement for a method of killing other carcinoma cells...." The claims have been amended to recite a "method to kill breast cancer cells or other carcinoma cells expressing the same target antigens." This amendment is consistent with what the Examiner has deemed to be enabled by the specification. Accordingly, withdrawal of the rejection is respectfully requested.

Claims 1, 3, 6-8, 21 and 25

Claims 1, 3, 6-8, 21 and 25 have been rejected under 35 USC 112, first paragraph, as lacking an enabling specification. Applicants traverse the rejection to the extent it is maintained.

The Examiner stated that the specification is enabling for a method of killing cancer cells in a cell population where the cell population is administered or contacted with immunotoxins, but is not enabling for a method where the cell population is exposed to immunotoxins. The claims have been amended to recite a method where the cell population is "incubated." Support for such an amendment can be found, for example, in Example 1. Applicant is open to amending the claims to recite "contacting" if the Examiner maintains the rejection. However, one skilled in the art would understand that incubation of an immunotoxin with a cell population would result in contact between the immunotoxin and the cells. Withdrawal of the rejection is respectfully requested.

Claims 1, 3, 6-8, 14, 21 and 25

Claims 1, 3, 6-8, 14, 21 and 25 have been rejected under 35 USC 112, first paragraph, as lacking an enabling specification. Applicants traverse the rejection to the extent it is maintained.

The Examiner stated that the specification is not enabling for the use of PE toxin fragments. The Examiner contends that not every fragment of a toxin would be active in killing cells and that a non-active fragment would not function as claimed. Applicants assert that one of skill in the art, upon reading the specification, would understand that the toxin fragments recited in the claims refer to active toxin fragments. Similarly, one skilled in the art would understand that an active fragment of PE would be a fragment containing the protein synthesis inhibiting part of the PE toxin. For purposes of clarification, the claims have been amended to recite "active" toxin fragments. Withdrawal of the rejection is respectfully requested.

Claims 15-17 and 19-20

Claims 15-17 and 19-20 have been rejected under 35 USC 112, first paragraph, as lacking an enabling specification. Applicants traverse the rejection to the extent it is maintained.

The Examiner stated that the specification, "while being enabling for an *ex vivo* method for killing malignant cells in a cell population comprising nucleated cells in peripheral blood and bone marrow, does not reasonably provide enablement for an *ex vivo* method for killing malignant cells in a cell population." The claims have been amended to recite a "cell population comprising nucleated peripheral blood cells or bone marrow cells." Accordingly, withdrawal of the rejection is requested.

Claims 22-24

Claims 22-24 have been rejected under 35 USC 112, first paragraph, as lacking an enabling specification for the reasons set forth in Paper No. 16, Section 4, pages 2-3. Applicant traverses the rejection.

The Examiner stated, "the arguments drawn to the rejection of claims 1, 3, and 6-8 drawn to *in vivo* treatment are relevant to the instant rejection." Applicant asserts that the specification provides support for an *in vivo* us of the method as claimed. As indicated above at pages 6-7 of this response:

> Examples 3 and 4 at pages 26-28 of the application, for example, show efficacy of immunotoxins, MOC31-PE and BM7-PE, in an appropriate animal model. In these examples, intravenously administered immunotoxins increased survival time of rats injected with human breast cancer cells lines into the left cardiac ventricle and into bone marrow. As

additional support for the proposition that the immunotoxins MOC31-PE and BM7-PE are effective in an appropriate *in vivo* model, Applicant submits herewith a copy of a journal article (Int. J. Cancer 88: 970-976, 2000) demonstrating the effectiveness of the immunotoxins in a nude rat model. One skilled in the art would understand the effectiveness of the claimed invention given the *in vivo* data in the application showing the effectiveness of the individual immunotoxins in rat models in combination with the *in vitro* data showing 1) the high specificity of the antibodies, 2) the effectiveness of the combined immunotoxin approach, and 3) the low toxicity of the combined immunotoxin approach for non-maligant cells. This combination of *in vitro* and *in vivo* data reaches well beyond speculation. One skilled in the art would understand that two immunotoxins, each independently effective in vivo, would be effective in combination, especially if *in vitro* studies showed the combination to be surprisingly effective.

Withdrawal of the rejection is respectfully requested.

Claims 1, 3, 7, 15-21 and 25

Claims 1, 3, 7, 15-21 and 25 have been rejected under 35 USC 112, second paragraph as being indefinite. Applicants traverse the rejection to the extent that it is maintained.

Claims 1 and 3 were rejected because claim 1 recites "the cell population is exposed to." The Examiner deemed this language confusing because "it is unclear whether cell population is actually combined with the two immunotoxins, whether the immunotoxins are administered or whether the two immunotoxins are simply placed in proximity to the cell population." The claim 1 has been amended to recite that the cell population is incubated with the immunotoxins. As states above, one skilled in the art would understand the term "incubate" and that incubation of an immunotoxin with a cell population would result in contact between the immunotoxin and the cells. As the term "incubate" is clear and definite in the context used in the claims, withdrawal of the rejection is respectfully requested.

Claims 3 and 16 were deemed indefinite because they recited "595A6." As indicated above, the calims have been amended to replace "595A6" with "BM7." Because, as indicated above, BM7 is clear and definite, withdrawal of the rejection is respectfully requested.

Claim 7 was found indefinite for reciting "especially in case of malignant spread to tissues such as bone and bone marrow" and "such as." Claim 7 has been amended to delete thses phrases and their accompanying text. New dependent claims 26 and 27 now recite the relevant

portions deleted from claim 7. Applicant asserts that claim 7 as amended is definite and requests that the rejection be withdrawn.

Claims 15-20 were deemed indefinite because the phrases "obtaining the population of cells *ex vivo*" and "wherein the cell population is obtained *ex vivo* from the patient" in claims 15 and 17, respectively, are "confusing because it is unclear how the cell population can be obtained outside the body of the cancer patient when they must be obtained inside the body..." Claim 15 has been amended and clarified to recite that the population of cells is contacted with the immunotoxins *ex vivo*. The reference to ex vivo in claim 17 has been deleted. Applicant asserts that the claims as now amended are clear and definite. Withdrawal of the rejection is respectfully requested.

Claims 21 and 25 were found indefinite because they recite the phrase "low toxicity" and "low is a relative term which renders the claim indefinite." Claim 25 has been canceled and claim 21 has been amended to recite, " relatively high toxicity to cancer or carcinoma cells and relatively low toxicity to CD34+ cells in the population." Support for the amendment can be found, for example, at page 6, lines 13-16 of the specification where it is stated that the immunotoxins were able to kill all cancer cells without significantly affecting the normal cells. As the Examiner stated "low" is a relative term. Amending the claim to give a reference point for "low toxicity" renders the claim definite as it states to what low toxicity is relative. As such Applicant asserts the claim is now definite and requests withdrawal of the rejection.

Claims 21 and 25 were also deemed indefinite for reciting "two or more immunotoxins" because there was no antecedent basis in claim 1 from which both claims 21 and 25 depend. Claim 1 has been amended to recite " two or more immunotoxins" to provide proper antecedent basis. As indicated above, the specification at page 4 lines 8-10 provides support for this amendment. Withdrawal of the rejection in light of the amendment is respectfully requested.

Claims 23 and 25

Claims 23 and 25 have been rejected under 35 USC 112, fourth paragraph, as being of improper dependent form. Applicants traverse the rejection to the extent that it is maintained.

Claims 23 and 25 have been cancelled rendering the rejection moot. Thus, withdrawal of the rejection is requested.

New Grounds of Rejection - Claim Rejections - 35 U.S.C. § 103

Claims 15 and 17-20 were rejected under 35 USC 103 essentially for the same reasons as claims 1 and 14 as discussed above. That is, the claims stand rejected as allegedly being obvious over Lemoli et al. in view of Brugger et al., Parry et al., Bjorn et al., and US Patent No. 5, 185, 254. Applicant traverses the rejection.

As stated above, the claimed method provides surprising efficacy against malignant cells, which would not be predicted by the references cited by the Examiner. None of the references cited by the Examiner alone or in combination suggest that the combination of immunotoxins directed to EGP2 and MUC1 would prove more effective than the sum of each immunotoxin directed to either EGP2 or MUC1 alone. The present application shows this unexpected result (see, for example, page 11, lines 14-17 and table 4). The unexpected advantages of the claimed method were neither taught nor suggested by the references cited by the Examiner, alone or in combination. Because of the unexpected and surprising advantages of the claimed method over the art cited by the Examiner, Applicant asserts that the claimed invention is not obvious. Withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants respectfully assert that the claims 1, 3, 6-8, 13, and 14 -25, upon entry of this amendment, are in a condition for allowance, and earnestly solicit a notice to that effect.

Applicants believe all of the outstanding objection and rejections have been addressed. If the Examiner has any questions regarding the foregoing, it is respectfully requested that she call the undersigned.

Respectfully Submitted,

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Date 1/8/02

John J. Gresens
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JJG/KMC

Enclosures: 1) Int. J. Cancer 88: 970-976, 2000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Fodstad et al.	Examiner:	S. Ungar
Serial No.:	09/125,751	Group Art Unit:	1642
Filed:	October 30, 1998	Docket No.:	7885.55USWO
Title:	METHOD OF KILLING TARGET CELLS IN HARVESTED CELL POPULATIONS WITH ONE OR MORE IMMUNOTOXINS		

MARKED UP COPY OF SPECIFICATION AND CLAIMS SHOWING AMENDMENTS

In the specification:

At page 4, line 12, the following paragraph has been inserted as follows:

In one aspect, the invention provides a method to kill breast cancer or other carcinoma cells expressing the same antigens in a cell population comprising nucleated cells harvested from peripheral blood, or CD-34+ cells selected from the above nucleated cells, or other immature/early progenitor cells from blood containing multipotent stem cells, wherein the cell population is exposed to a combination of two immunotoxins, wherein each immunotoxin is composed of a conjugate between an antibody and a cell toxin, fragments of antibodies and toxin, or recombinantly produced antibodies, toxins, immunotoxins or fragments thereof, wherein the antibodies are directed to epitopes on the antigen EGP2 expressed by the gene GA733 and to epitopes on the antigen expressed by the genes MUC1, MUC2 or MUC 3, respectively or a combination of these, and the toxin is Pseuctomonas exotoxin A.

In the claims:

Claims 13, 18, 23 and 25 have been cancelled.

Claims 1, 3, 6-8, 14-17, 19, and 21-22 have been amended as follows:

1. (Amended) Method to kill breast cancer cells or other carcinoma cells expressing the same target antigens in a cell population selected from the group consisting of cells comprising nucleated cells in peripheral blood and bone marrow cells comprising CD-34$^+$ cells selected from the above nucleated cells, the method comprising:

[wherein] incubating the cell population [is exposed to] with a combination of two or more immunotoxins, wherein each immunotoxin [is composed of] comprises a conjugate between an antibody [and a cell toxin,] or antigen binding antibody fragments and a cell toxin or active toxin fragments, or a recombinantly produced antibodies [,] or antigen binding antibody fragments, and toxins [,] or active toxin fragments [, immunotoxins or fragments thereof], wherein the antibodies or antigen binding antibody fragments are directed to epitopes on the antigen EGP2 expressed by the gene GA733-2 and to epitopes on the antigen expressed by the MUC1 gene and the toxin is Pseudomonas exotoxin A.

3. (Amended) [Method] The method according to claim 1, [characterized in that] wherein the [used] antibodies are MOC31 and [595A6] BM7, or antigen binding fragments thereof.

6. (Amended) [Method] The method according to claim 1 wherein said [exposure] incubating consists of administering the [specific] immunotoxins in vivo.

7. (Amended) [Method] The method according to claim 6, [characterized in that] wherein the immunotoxins are administered systemically [, especially in case of malignant spread to tissues such as bone and bone marrow].

8. (Amended) [Method] The method according to claim 6, [characterized in that] wherein the immunotoxins are administered directly into [the] a tumor or [in the pleural and abdominal cavities] intrapleurally of intra-abdominally.

13

~~14~~. (Amended) The method of claim 1, wherein said [exposure] incubating consists of administering the immunotoxins *ex vivo*.

14

~~15~~. (Amended) A method for killing [malignant cells] breast cancer cells or other carcinoma cells expressing the same antigens in a cell population comprising nucleated peripheral blood cells or bone marrow cells, the method comprising

obtaining the population of cells [*ex vivo*] that contains the [malignant cells] breast cancer cells or other carcinoma cells expressing the same antigens;

contacting the population of cells *ex vivo* with [at least] two or more immunotoxins, wherein a first immunotoxin comprises a PE molecule conjugated to an antibody or an antibody fragment capable of binding an EGP2 antigen which is expressed by a GA733-2 gene and a second immunotoxin comprising a PE molecule conjugated to an antibody or an antibody fragment capable of binding an antigen encoded by the MUC1, MUC2, or MUC3 gene.

15

16. (Amended) The method according to claim 15, wherein the first immunotoxin comprises a PE molecule conjugated to a MOC31 antibody or an antigen-binding antibody fragment thereof, and the second immunotoxin comprises a PE molecule conjugated to a [595A6] BM7 antibody or an antigen-binding antibody fragment thereof.

16

17. (Amended) The method according to claim 15, wherein the cell population is obtained [*ex vivo*] from a cancer patient.

18

19. (Amended) The method according to claim [18] 15, wherein the cell population comprises CD34+ cells

20

21. (Amended) The method according to claim 1 wherein treatment of the cell population with the two or more immunotoxins causes relatively high toxicity to cancer or carcinoma cells and relatively low toxicity to CD34+ cells in the population.

21

22. (Amended) A method for killing [malignant cells] breast cancer cells or other carcinoma cells expressing the same antigens in a patient, the method comprising

admistering to the patient a therapeutically effective amount of [at least] two or more immunotoxins, wherein a first immunotoxin comprises a PE molecule conjugated to an antibody or an antibody fragment capable of binding an EGP2 antigen which is expressed by a GA733-2 gene and a second immunotoxin comprises a PE molecule conjugated to an antibody or an

antibody fragment capable of binding an antigen encoded by the MUC1, MUC2, or MUC3 genes.

Claims 26 and 27 are new.

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